REMARKS

Claims 1-19 are pending and under examination in the subject application. Applicants have hereinabove canceled without disclaimer or prejudice claim 19. Accordingly, upon entry of the Amendment, claims 1-18 will be pending and under examination.

Restriction Requirement

The Examiner stated: "Applicants elected the synergistic combination of C_6-ceramide and taxol with traversed in Paper No. 6. Claims are being examined as they read on the elected combination. Applicants' remarks are noted but one synergistic combination of drugs is patentably distinct from another synergistic combination of drugs and will support a separate patent."

In response, applicants maintain the previous election of the enhanced combination of C6-ceramide, as the ceramide, and paclitaxel, as the antitumor chemotherapeutic agent, with traverse.

Rejection under 35 U.S.C. 112, first paragraph

Claims 1, 2 and 4-18

The Examiner rejected claims 1, 2 and 4-18 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific tumor and/or cancer disclosed, does not reasonably provide enablement for the term "tumor" and/or "tumor cells" and "cancer". The Examiner stated: "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in

scope with these claims. The terms "tumor cells" in claims 1, 4-11, 16 and 18, "tumor" in claims 2, 4-10 and 17 and "cancer" in claims 11-15 and 19 lack clear exemplary support in the specification as filed."

The Examiner also stated: "The cancer therapy art remains highly unpredictable, and no examples exist for efficacy of a combination of drugs against cancers or tumors generally. Therefore, based on the unpredictable nature of the invention and state of the prior art, lack of guidance and working example, and extreme breadth of the claims, one skilled in the art could not use the entire scope of the claimed invention without undue experimentation."

In response, applicants respectfully traverse the above-stated rejection under 35 U.S.C. 112, first paragraph and maintain that the scope of claims 1, 2 and 4-18 is enabled by the subject specification.

Applicants respectfully direct the Examiner's attention to the First Series of Experiments of the specification, inter alia at page 15, lines 7-23, which describes enhanced induction of apoptosis of Jurkat, a leukemic T cell line, which is a type of cancer.

Applicants also respectfully direct the Examiner's attention to the Second Series of Experiments of the specification inter alia at page 32, lines 33 through page 33, line 9, and the Third Series of

Experiments of the specification, inter alia at page 33, line 37 through page 34, line 5, and page 42, lines 22-30, which describes a synergistic growth inhibition, i.e. a decline in tumor size of human squamous carcinoma cells (Tu138), a type of neoplastic (cancer) cell line, and enhanced apoptosis after injection of paclitaxel and ceramide.

Applicants further respectfully direct the Examiner's attention to the Fourth Series of Experiments of the specification, inter alia Table 2, at page 52, lines 8-23, which summarizes the percent growth inhibition of a variety of human cancer cell lines by paclitaxel and ceramide; the human cancer cell lines tested for growth inhibition were human neoplastic cell lines HT29 (colon cancer), Jurkat (a leukemic T cell line), LnCaP (prostate cancer), PC-3 (hormone refractory prostate cancer), RWP-2 (pancreatic cancer), and TU138 (head and neck squamous carcinoma), as well as and MCF-7 tumors (a breast cancer cell line) in the Fifth Series of Experiments.

Therefore, the subject specification provides ample exemplary support and enablement for a human acute T cell leukemia as well as a variety of solid tumor cancer cell lines, i.e. various "tumors", "tumor cells" and cancers". Accordingly, applicants maintain the presently pending claims should not be limited to the specific tumor and/or cancer disclosed.

Accordingly, applicants respectfully request that the Examiner

reconsider and withdraw the above-stated rejection under 35 U.S.C. § 112, first paragraph.

Claims 1-13 and 15

Claims 1-13 and 15 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific antitumor chemotherapeutic agent and (sic) ceramide disclosed, does not reasonably provide enablement for the terms "antitumor chemotherapeutic agent" and "a ceramide". The Examiner stated: "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The terms "antitumor chemotherapeutic agent" in claims 1-6 and 8-13, and 15 and "a ceramide" in claims 1-5 and 7-13 lack clear exemplary support in the specification as filed."

In response, applicants respectfully traverse the above-stated rejection under 35 U.S.C. 112, first paragraph and maintain that the subject specification is enabling for the terms "antitumor chemotherapeutic agent" in claims 1-6 and 8-13 and "a ceramide" in claims 1-5 and 7-13.

Applicants respectfully direct the Examiner's attention to the subject specification at page 9, lines 29-34, wherein "ceramide" is defined as "any N-acylsphingosine". The specification states that ceramides include sphingolipids in which the sphingosine is acylated with a fatty acid acyl CoA derivative to form an N-

acylsphingosine, ceramide may be either naturally occurring or chemically synthesized, and preferably, the carbon chain length is less than 18 carbons. Examples of ceramides provided by the subject specification include C6-ceramide (N-hexanoyl-D-sphingosine), which is used in experiments described in the subject specification, C2-ceramide, C8-ceramide, and C16-ceramide. Accordingly, applicants maintain that the term "ceramide" is fully enabled by the subject specification.

Applicants further respectfully direct the Examiner's attention to the subject specification at page 11, line 35 through page 12, line 9, wherein the "antitumor chemotherapeutic agent" is described as paclitaxel or compounds structurally related to the paclitaxel family of compounds, e.g. alkaloids, and also "include but are not limited to chemotherapeutic agents such as doxorubicin, cis-platin, cyclophosphamide, etoposide, vinorelbine, vinblastin, tamoxifen, colchinin, 2-methoxyestradiol." In further embodiments of the methods of the subject invention, "the paclitaxel may be used together with another antitumor chemotherapeutic" and "combinations of any of the above-listed antitumor chemotherapeutic agents may be used". Accordingly, applicants maintain that the term "antitumor chemotherapeutic agent" is fully enabled by the subject specification.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the above-stated rejection under 35 U.S.C. §103(a).

Rejection under 35 U.S.C. 112, second paragraph

The Examiner rejected claims 14 and 19 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that claims 14 and 19 are improperly drawn to the same method and required correction.

In response, applicants have hereinabove canceled without disclaimer or prejudice claim 19. Applicants maintain that the cancellation of claim 19 obviates the Examiner's above-stated rejection and, therefore, respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. 112, second paragraph.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 1-19 under 35 U.S.C. §103(a) as being unpatentable over the WO 94/04541 reference taken with the Jayadev et al. reference of record. The Examiner stated: "WO 94/04541 reference teaches the synergistic combination of taxol and sphingosine, the core compound of the ceramide claimed, (see claim 25 and ABSTRACT) for treating cancer. The Jayadev et al. reference teaches the C_6-ceramide as an anticancer agent. The **references do not teach the combination of C_6-ceramide and taxol**. (Applicants' emphasis) Accordingly, one skilled in this art would be motivated to substitute the C_6-ceramide for the sphingosine in the primary reference synergistic combination since the core structure are the

same and both compound are anticancer agents.

In response, applicants respectfully traverse the above-stated rejection and maintain that claims 1-19 are not obvious under 35 U.S.C. §103(a) over WO 94/04541, published PCT International Application entitled "Protein Kinase Inhibitors and Related Compounds Combined with Taxol" (Abraham et al., March 3, 1994) in combination with Jayadev et al.

Applicants respectfully direct the Examiner's attention to pages 108 and 667 of Webster's Medical Desk Dictionary, (1986) Merriam-Webster Inc. Springfield, MA, attached hereto as **Exhibit A**, in which a sphingosine is defined as "an unsaturated amino diol $C_{18}H_{37}NO_2$ obtained by hydrolysis of various sphingomyelins, cerebrosides and gangliosides", whereas a ceramide is defined as "any of a group of amides formed by linking a fatty acid to a sphingosine and found widely but in small amounts in plant and animal tissue." Applicants note that there are distinct differences in the structure and function of sphingosine and ceramide, as follows: 1) although both sphingosine and ceramide have a double bond in the 4, 5 position (a trans 4,5 bond), if the double bond of ceramide is saturated, ceramide will not work, whereas, if the double bond of sphingosine is saturated, sphingosine will work, accordingly, the double bond is necessary in the former and not the latter for proper functioning of the compound -- so even if sphingosine is the core compound of ceramide the mode of action differs; 2) sphingosine has been shown to be a

PKC inhibitor [in this regard, applicants note the title of WO 94/04541, is "Protein Kinase Inhibitors and Related Compounds Combined with Taxol"], whereas ceramide has not, therefore, the mechanism of action of the respective compounds differs; 3) the kinetics of sphingosine are very rapid, whereas, those of ceramide are slow; 4) sphingosine and ceramide are distributed in the cell differently, therefore, one of skill would not substitute sphingosine, the core compound of ceramide, for "ceramide" in any of the claimed methods of increasing apoptosis and decreasing size of a tumor with a reasonable expectation of success. Applicants will attempt to shortly submit a Supplemental Communication to provide literature in support of the aforementioned for the Examiner's review.

Applicants note further that WO 94/04541 merely lists the term "sphingosine" at pages 4, 9, and in claims 25 and 29, without providing any experimental data as to whether **sphingosine** and taxol may be used for treatment of cancer. Therefore, at most, WO 94/04541 provides an invitation to one of skill to perform experiments using **sphingosine** and taxol to determine if such a combination would result in successful treatment of tumors or cancers. However, WO 94/04541 provides **no** suggestion or motivation to one of skill in the art to use ceramide (instead of sphingosine) and taxol. Therefore, absent some suggestion or teaching in WO 94/04541, sphingosine and ceramide are not interchangeable, and the combination of Jayadev et al. with WO 94/04541 does not cure the defect of WO 94/04541 of failing to suggest ceramide for use in

combination with taxol in methods of treating cancer and tumors. Jayadev et al. study only the role of ceramide in cell cycle arrest and as stated on page 2051, column 2, second full paragraph, Jayadev et al. "identify a novel role for ceramide in regulating cell cycle progression whereby ceramide induces a significant G0/G1 arrest". Jayadev et al. also state in the same paragraph that "ceramide may function as a proximal sensor and transducer of cell deprivation/insult/injury with the ability to launch distinct programs of cell suppression (growth arrest and apoptosis), the outcome of which may depend on whether other modulatory signals ... are also activated." Therefore, Jayadev et al. do not per se teach that C_6-ceramide may be used as an anticancer agent. Moreover, Jayadev et al. do not teach or suggest that ceramide be combined with at least one antitumor chemotherapeutic agent, to arrive at a method for increasing apoptosis in tumor cells or a method of decreasing a size of a tumor, as claimed.

To establish a prima facie case for obviousness, three criteria must be met: 1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. 2) There must be a reasonable expectation of success. 3) The prior art reference (or references when combined) must teach or suggest <u>all</u> the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the applicant's

disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), see also M.P.E.P. §904.01(d).

As discussed above, WO 94/04541 merely lists the term "sphingosine" at pages 4, 9, and in claims 25 and 29, without providing any experimental data as to whether **sphingosine** and taxol may be used for treatment of cancer. WO 94/04541 does not teach or suggest use of ceramide as set forth in the claimed methods.

As discussed above Jayadev et al. "identify a novel role for ceramide in regulating cell cycle progression whereby ceramide induces a significant G0/G1 arrest". Jayadev et al. do not teach or suggest any methods comprising contacting tumor cells with an effective amount of at least one antitumor chemotherapeutic agent **and** an effective amount of a ceramide, sequentially or concomitantly, as claimed, so as to increase apoptosis in tumor cells or to decrease the size of a tumor. (emphasis added) Accordingly, the combination of references does not teach or suggest any modification of the reference or to combine reference teachings to arrive at the claimed methods as set forth in claims 1-19.

Neither WO 94/04541 nor Jayadev et al. provide any motivation or suggestion to practice the invention as described in the subject application. Accordingly, the combination of references does not teach or suggest all of the claimed limitations of the subject application, as required under 35 U.S.C. §103(a). Accordingly,

applicants maintain that the claimed invention is not obvious over WO 94/04541 and Jayadev et al.

Applicants also wish to direct the Examiner's attention to In re Rouffet, 47 USPQ2d 1453, 1457-1458 (Fed. Cir. 1998) which states:

> "To prevent the use of hindsight, this court requires the examiner to show a motivation to combine the references that create the obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select elements from the cited prior art for combination in the manner claimed."

The Court further states that "the Board did not rely upon any of the three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art. Rather, it relied upon the high level of skill in the art to provide the necessary motivation. The Board did not explain what specific understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested the combination." In re Rouffet, 47 USPQ2d 1453, 1458. Therefore, a high level of skill in the art, without more, cannot supply the required motivation to combine references, and does not overcome absence of any actual suggestion to combine.

At page 4 of the September 28, 2000 Office Action, the Examiner states that "the references do not teach the combination of C_6-ceramide and taxol. (applicants' emphasis) Accordingly, one skilled in the art would be motivated to substitute the C_6-ceramide for the sphingosine in the primary reference synergistic combination since the core structures (sic) are the same and both compounds are anticancer drugs." The Examiner has not shown why one of skill would, using the teachings of WO 94/04541 and Jayadev et al., select C_6-ceramide and taxol to contact cells to arrive at a method of increasing apoptosis in tumor cells or a method to decrease the size of a tumor, as claimed, since: 1) WO 94/04541, which makes no mention of C_6-ceramide and at most invites one of skill to perform experiments using **sphingosine** and taxol to determine if such a combination would result in successful treatment of tumors or cancers, and 2) Jayadev et al. identify a novel role for ceramide in regulating cell cycle progression whereby ceramide induces a significant G0/G1 arrest, but do not teach or suggest its use in methods of increasing apoptosis or methods to decrease the size of a tumor and clearly do not suggest combining ceramide with taxol for such methods. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the above-stated rejection of claims 1-19 under 35 U.S.C. § 103(a).

In summary, in view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the grounds of rejection in the September 28, 2000 Office

Action and earnestly solicit allowance of the claims now pending in the subject application, namely, claims 1-18.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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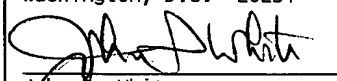

12/28/00

John P. White
Reg. No. 28,678

Date

Webster's Medical Desk Dictionary

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sense organ to the brain or spinal cord) : AFFERENT — **cen·trip·e·tal·ly** \-ᵊl-ē\ *adv*

cen·tro·lec·i·thal \ˌsen-trō-'les-ə-thəl\ *adj, of an egg* : having the yolk massed centrally and surrounded by a thin layer of clear cytoplasm — compare ISOLECITHAL, TELOLECITHAL

cen·tro·mere \'sen-trə-ˌmi(ə)r\ *n* : the point on a chromosome by which it appears to attach to the spindle in mitosis — called also *kinetochore* — **cen·tro·mer·ic** \ˌsen-trə-'mi(ə)r-ik, -'mer-\ *adj*

cen·tro·plasm \'sen-trō-ˌplaz-əm\ *n* : CENTRAL BODY 2

cen·tro·some \'sen-trə-ˌsōm\ *n* 1 : CENTRIOLE 2 : the centriole-containing region of clear cytoplasm adjacent to the cell nucleus — **cen·tro·so·mic** \ˌsen-trə-'sō-mik\ *adj*

cen·tro·sphere \'sen-trə-ˌsfi(ə)r\ *n* : the differentiated layer of cytoplasm surrounding the centriole within the centrosome

cen·trum \'sen-trəm\ *n, pl* **centrums** *or* **cen·tra** \-trə\ 1 : the center esp. of an anatomical part 2 : the body of a vertebra

Cen·tru·roi·des \ˌsen-trə-'rȯi-(ˌ)dēz\ *n* : a genus of scorpions containing the only forms dangerous to man that occur in the U.S.

ce·pha·eline \se-'fā-ə-ˌlēn, -lən\ *n* : a colorless crystalline alkaloid $C_{28}H_{38}N_2O_4$ extracted from ipecac root

Cepha·elis \ˌsef-ə-'ē-ləs\ *n* : a large genus of tropical shrubs and trees (family Rubiaceae) with small tubular flowers crowded into dense heads that includes ipecac

ceph·a·lad \'sef-ə-ˌlad\ *adv* : toward the head or anterior end of the body

ceph·a·lal·gia \ˌsef-ə-'lal-j(ē-)ə\ *n* : HEADACHE

ceph·a·lex·in \ˌsef-ə-'lek-sən\ *n* : a semisynthetic cephalosporin $C_{16}H_{17}N_3O_4S$ with a spectrum of antibiotic activity similar to the penicillins

ceph·al·he·ma·to·ma *or chiefly Brit* **ce·phal·hae·ma·to·ma** \ˌsef-əl-ˌhē-mə-'tō-mə\ *n, pl* **-mas** *or* **-ma·ta** \-mət-ə\ : a blood-filled tumor or swelling beneath the pericardium that occurs frequently in newborn infants as a result of injury (as by forceps) during birth

ce·phal·ic \sə-'fal-ik\ *adj* 1 : of or relating to the head 2 : directed toward or situated on or in or near the head — **ce·phal·i·cal·ly** \-i-k(ə-)lē\ *adv*

cephalic flexure *n* : the middle of the three anterior flexures of an embryo in which the front part of the brain bends downward in an angle of 90 degrees — called also *cranial flexure*

cephalic index *n* : the ratio multiplied by 100 of the maximum breadth of the head to its maximum length — compare CRANIAL INDEX

cephalic vein *n* : any of various superficial veins of the arm; *specif* : a large vein of the upper arm lying along the outer edge of the biceps muscle and emptying into the axillary vein

ceph·a·lin \'kef-ə-lən, 'sef-\ *also* **keph·a·lin** \'kef-\ *n* : PHOSPHATIDYLETHANOLAMINE

ceph·a·li·za·tion *or Brit* **ceph·a·li·sa·tion** \ˌsef-ə-lə-'zā-shən\ *n* : an evolutionary tendency to specialization of the body with concentration of sensory and neural organs in an anterior head

ceph·a·lo·cau·dal \ˌsef-ə-lō-'kȯd-ᵊl\ *adj* : proceeding or occurring in the long axis of the body esp. in the direction from head to tail — **ceph·a·lo·cau·dal·ly** \-ᵊl-ē\ *adv*

Ceph·a·lo·chor·da \-'kȯrd-ə\ *n pl* : a subphylum or other division of Chordata consisting of the lancelets in which the notochord extends to the anterior as well as the posterior end of the body

Ceph·a·lo·chor·da·ta \-ˌkȯr-'dāt-ə, -'dāt-ə\ *syn of* CEPHALOCHORDA

ceph·a·lo·gram \'sef-ə-lə-ˌgram\ *n* : a radiograph of the head esp. for orthodontic purposes

ceph·a·lom·e·ter \ˌsef-ə-'läm-ət-ər\ *n* : an instrument for measuring the head

ceph·a·lom·e·try \ˌsef-ə-'läm-ə-trē\ *n, pl* **-tries** : the science of measuring the head — **ceph·a·lo·met·ric** \-lō-'me-trik\ *adj*

ceph·a·lo·pel·vic disproportion \ˌsef-ə-lō-ˌpel-vik-\ *n* : a condition in which a maternal pelvis is small in relation to the size of the fetal head

Ceph·a·lop·o·da \ˌsef-ə-'läp-əd-ə\ *n pl* : a class of mollusks including the squids, cuttlefishes, and octopuses that have a tubular siphon under the head, a group of muscular arms around the front of the head which are usu. furnished with suckers, highly developed eyes, and usu. a bag of inky fluid which can be ejected for defense or concealment — **ceph·a·lo·pod** \'sef-ə-lə-ˌpäd\ *adj or n* — **ceph·a·lop·o·dan** \ˌsef-ə-'läp-əd-ən\ *adj or n*

ceph·a·lor·i·dine \ˌsef-ə-'lȯr-ə-ˌdēn, -'lär-\ *n* : a broad-spectrum antibiotic $C_{19}H_{17}N_3O_4S_2$ derived from cephalosporin

ceph·a·lo·spo·rin \ˌsef-ə-lə-'spōr-ən, -'spȯr-\ *n* : any of several antibiotics produced by an imperfect fungus of the genus *Cephalosporium*

Ceph·a·lo·spo·ri·um \-'spōr-ē-əm, -'spȯr-\ *n* : a form genus of imperfect fungi with conidia held together by a slimy secretion in more or less spherical heads at the ends of the fertile branches

ceph·a·lo·thin \'sef-ə-lə-(ˌ)thin\ *n* : a semisynthetic broad-spectrum antibiotic $C_{16}H_{15}N_2NaO_6S_2$ that is an analogue of a cephalosporin and is effective against penicillin-resistant staphylococci

ceph·a·lo·tho·ra·cop·a·gus \ˌsef-ə-ˌlō-ˌthōr-ə-'käp-ə-gəs, -ˌthȯr-\ *n, pl* **-a·gi** \-ˌgī, -ˌgē\ : a teratological monster consisting of twins joined at the head, neck, and thorax

CER *abbr* conditioned emotional response

ce·ra al·ba \ˌsir-ə-'al-bə\ *n* : WHITE WAX

ce·ra·ceous \sə-'rā-shəs\ *adj* : resembling wax

ce·ra fla·va \ˌsir-ə-'flāv-ə, -'flā-və\ *n* : YELLOW WAX

cer·amide \'sir-ə-ˌmīd\ *n* : any of a group of amides formed by linking a fatty acid to sphingosine and found widely but in small amounts in plant and animal tissue

cer·amide·tri·hexo·si·dase \ˌsir-ə-ˌmīd-ˌtrī-ˌhek-sə-'sī-ˌdās, -ˌdāz\ *n* : an enzyme that breaks down ceramidetrihexoside and is deficient in individuals affected with Fabry's disease

cer·amide·tri·hexo·side \-(ˌ)trī-'hek-sə-ˌsīd\ *n* : a lipid that accumulates in body tissues of individuals affected with Fabry's disease

ce·rate \'si(ə)r-ˌāt\ *n* : an unctuous preparation for external use consisting of wax or resin or spermaceti mixed with oil, lard, and medicinal ingredients

cer·a·to·hy·al \ˌser-ə-(ˌ)tō-'hī-əl\ *or* **cer·a·to·hy·oid** \-'hī-ˌȯid\ *n* : the smaller inner projection of the two lateral projections on each side of the hyoid bone in man — called also *lesser cornu*; compare THYROHYAL

Cer·a·to·phyl·lus \ˌser-ə-(ˌ)tō-'fil-əs\ *n* : a genus of fleas formerly coextensive with the family Dolichopsyllidae but now restricted to some parasites of birds

cer·car·ia \(ˌ)sər-'kar-ē-ə, -'ker-\ *n, pl* **-i·ae** \-ē-ˌē\ : a usu. tadpole-shaped larval trematode worm produced in a molluscan host by a redia — **cer·car·i·al** \-ē-əl\ *adj*

cer·clage \ser-'kläzh, (ˌ)sər-\ *n* : any of several procedures for increasing tissue resistance in a functionally incompetent uterine cervix that usu. involve reinforcement with an inert substance esp. in the form of sutures near the internal opening

Cer·com·o·nas \(ˌ)sər-'käm-ə-nəs\ *n* : a genus of commensal or coprophilous flagellated protozoans (order Protomonadina) having two flagella

Cer·co·pi·the·ci·dae \ˌsər-kō-pə-'thē-sə-ˌdē, -'thē-kə-\ *n pl* : a family of primates that includes all the Old World monkeys except the anthropoid apes and is coextensive with a superfamily (Cercopithecoidea) — **cer·co·pith·e·coid** \-'pith-ə-ˌkȯid, -pə-'thē-\ *adj or n*

Cer·co·pi·the·cus \-pə-'thē-kəs, -'pith-ə-\ *n* : a genus of the family Cercopithecidae that includes slender long-tailed African monkeys comprising the guenons and related forms with cheek pouches and ischial callosities

cer·cus \'sər-kəs\ *n, pl* **cer·ci** \'sər-ˌsī, -ˌkī\ : either of a pair of simple or segmented appendages at the posterior end of various arthropods

cere \'si(ə)r\ *vt* **cered; cer·ing** : to wrap in or as if in a cerecloth

ce·rea flex·i·bil·i·tas \ˌsir-ē-ə-ˌflek-sə-'bil-ə-ˌtas, -ˌtās\ *n* : the capacity (as in catalepsy) to maintain the limbs or other bodily parts in whatever position they have been placed

[1]ce·re·al \'sir-ē-əl\ *adj* : relating to grain or to the plants that produce it; *also* : made of grain

[2]cereal *n* 1 : a plant (as a grass) yielding farinaceous grain suitable for food; *also* : its grain 2 : a prepared foodstuff of grain

cerebellar artery *n* : any of several branches of the basilar and

can result from various nutritional or environmental factors or be induced artificially by use of a lysozyme

sphinc·ter \'sfiŋ(k)-tər\ *n* : an annular muscle surrounding and able to contract or close a bodily opening — see ANAL SPHINCTER — **sphinc·ter·al** \-t(ə-)rəl\ *adj*

sphincter ani ex·ter·nus \-'ā-ˌnī-ik-'stər-nəs\ *n* : ANAL SPHINCTER a

sphincter ani in·ter·nus \-in-'tər-nəs\ *n* : ANAL SPHINCTER b

sphinc·ter·ec·to·my \ˌsfiŋk-tər-'ek-tə-mē\ *n, pl* **-mies** : surgical excision of a sphincter

sphinc·ter·ic \sfiŋ(k)-'ter-ik\ *adj* : of, relating to, or being a sphincter ⟨~ control⟩ ⟨a ~ muscle⟩

sphincter of Od·di \-'äd-ē\ *n* : a complex sphincter closing the duodenal orifice of the common bile duct

Oddi, Ruggero (1864–1913), Italian physician. While studying in vivo the action of the bile on digestion, Oddi discovered the sphincter of the common bile duct. He later measured the tone of the sphincter by perfecting an experimental device very similar to the device now used for the intraoperative manometry of the bile ducts.

sphinc·tero·plas·ty \'sfiŋk-tər-ə-ˌplas-tē\ *n, pl* **-ties** : plastic surgery of a sphincter ⟨anal ~⟩

sphinc·ter·ot·o·my \ˌsfiŋk-tər-'ät-ə-mē\ *n, pl* **-mies** : surgical incision of a sphincter

sphincter pu·pil·lae \-pyü-'pil-ē\ *n* : a broad flat band of smooth muscle in the iris that surrounds the pupil of the eye

sphincter ure·thrae \-yù-'rē-thrē\ *n* : a muscle composed of fibers that arise from the inferior ramus of the ischium and that interdigitate with those from the opposite side of the body to form in the male a narrow ring of muscle around the urethra just distal to the apex of the prostate gland and in the female a ring of muscle more generally distributed around the urethra — called also *urethral sphincter*

sphincter va·gi·nae \-və-'jī-nē\ *n* : the bulbocavernosus of the female

sphin·go·lip·id \ˌsfiŋ-gō-'lip-əd\ *n* : any of a group of lipids (as sphingomyelins and cerebrosides) that yield sphingosine or one of its derivatives as one product of hydrolysis

sphin·go·lip·i·do·sis \-ˌlip-ə-'dō-səs\ *n, pl* **-do·ses** \-ˌsēz\ : any of various usu. hereditary disorders (as Gaucher's disease and Tay-Sachs disease) characterized by abnormal metabolism and storage of sphingolipids

sphin·go·my·elin \ˌsfiŋ-gō-'mī-ə-lən\ *n* : any of a group of crystalline phosphatides that are obtained esp. from nerve tissue and that on hydrolysis yield a fatty acid (as lignoceric acid), sphingosine, choline, and phosphoric acid

sphin·go·my·elin·ase \-'mī-ə-lə-ˌnās, -ˌnāz\ *n* : any of several enzymes that catalyze the hydrolysis of sphingomyelin and are lacking in some metabolic deficiency diseases (as Niemann-Pick disease) in which sphingomyelin accumulates in bodily organs (as the spleen and liver)

sphin·go·sine \'sfiŋ-gə-ˌsēn, -sən\ *n* : an unsaturated amino diol $C_{18}H_{37}NO_2$ obtained by hydrolysis of various sphingomyelins, cerebrosides, and gangliosides

sphyg·mic \'sfig-mik\ *adj* : of or relating to the circulatory pulse

sphyg·mo·gram \'sfig-mə-ˌgram\ *n* : a tracing made by a sphygmograph and consisting of a series of curves that correspond to the beats of the heart

sphyg·mo·graph \'sfig-mə-ˌgraf\ *n* : an instrument that records graphically the movements or character of the pulse

sphyg·mo·ma·nom·e·ter \ˌsfig-mō-mə-'näm-ət-ər\ *n* : an instrument for measuring blood pressure and esp. arterial blood pressure

sphyg·mo·ma·nom·e·try \-mə-'näm-ə-trē\ *n, pl* **-tries** : measurement of blood pressure by means of the sphygmomanometer

sphyg·mom·e·ter \sfig-'mäm-ət-ər\ *n* : an instrument for measuring the strength of the pulse beat

spi·ca \'spī-kə\ *n, pl* **spi·cae** \-ˌkē\ *or* **spicas** : a bandage that is applied in successive V-shaped crossings and is used to immobilize a limb esp. at a joint; *also* : such a bandage impregnated with plaster of paris ⟨a ~ cast applied at the hip⟩

spic·ule \'spik-(ˌ)yü(ə)l\ *n* : a minute slender pointed usu. hard body (as of bone)

spi·der \'spīd-ər\ *n* 1 : any of an order (Araneida) of arachnids having a body with two main divisions, four pairs of walking legs, and two or more pairs of abdominal spinnerets for spinning threads of silk used in making cocoons for their eggs, nests for themselves, or webs to catch prey 2 : SPIDER NEVUS ⟨an arterial ~⟩ 3 : an obstruction in the teat of a cow; *esp* : a small irregular horny growth resulting from irritation or bruising

spider nevus *n* : a nevus formed of dilated capillaries radiating from a central point like the legs of a spider

Spiel·mey·er–Vogt disease \'shpēl-ˌmī-ər-'fōkt-\ *n* : an inherited progressive fatal disorder of lipid metabolism having an onset at about five years of age and characterized by blindness, paralysis, and dementia — called also *juvenile amaurotic idiocy;* compare GAUCHER'S DISEASE, NIEMANN-PICK DISEASE, TAY-SACHS DISEASE

Spielmeyer, Walter (1879–1935), German neurologist. Spielmeyer is known for describing a method of microscopic examination of myelin sheaths of the nervous system (1911) and a juvenile form of amaurotic idiocy.

Vogt, Oskar (1870–1959), German neurologist. Vogt was the director and founder of two institutes for brain research in Germany. He undertook extensive research on brain structure, developing new views on brain architectonics. In 1920 he described a syndrome characterized by bilateral athetosis, walking difficulties, speech disorders, and excessive myelination of the nerve fibers of the corpus striatum.

spi·ge·lia \spī-'jē-l(ē-)yə\ *n* 1 *cap* : a large genus of American herbs (family Loganiaceae) with showy flowers 2 : PINKROOT

Spie·ghel \'spē-gəl\, **Adriaan van den (1578–1625),** Flemish anatomist. Spieghel was for many years professor of anatomy at Padua, Italy. He published a major treatise on human anatomy in 1627. He is also remembered for an introductory text on botany (1606). The genus *Spigelia* of herbs was named in his honor by Linnaeus in 1753.

spi·ge·lian hernia \spī-'jē-l(ē-)yən-\ *n, often cap S* : a hernia occurring along the linea semilunaris

spigelian lobe *n, often cap S* : CAUDATE LOBE

[1]spike \'spīk\ *n* : a change (as in voltage or potential difference) involving a sharp increase and fall or a recording of this: as **a** : the pointed element in the wave tracing in an electroencephalogram ⟨the ~ and dome pattern representing the discharges characteristic of petit mal epilepsy⟩ **b** : a sharp increase in body temperature followed by a rapid fall ⟨a fever with ~s to 103°⟩ **c** : the sharp increase and fall in the recorded action potential of a stimulated nerve cell that during the increasing phase corresponds to an inrush of sodium ions to the interior of the cell and during the decreasing phase corresponds to a slowing of the influx of sodium ions and to an increasing efflux of potassium ions to the exterior **d** : ACTION POTENTIAL

[2]spike *vt* **spiked; spik·ing** : to undergo a sudden sharp increase in (temperature or fever) usu. up to an indicated level ⟨one of the pathologists *spiked* a fever as high as 105°F —*Therapeutic Notes*⟩

spike·nard \'spīk-ˌnärd\ *n* 1 **a** : a fragrant ointment of the ancients **b** : an East Indian aromatic plant (*Nardostachys jatamansi*) from which spikenard is believed to have been derived 2 : an American herb of the genus *Aralia* (*A. racemosa*) whose dried rhizomes and roots have been used as a diaphoretic and aromatic

spike potential *n* 1 : SPIKE c 2 : ACTION POTENTIAL

spik·ing *adj* : characterized by recurrent sharp rises in body temperature ⟨a ~ fever⟩; *also* : resulting from a sharp rise in body temperature ⟨a ~ temperature of 105°⟩

spi·na \'spī-nə\ *n, pl* **spi·nae** \-ˌnē\ : an anatomical spine or spinelike process

spina bi·fi·da \-'bif-ə-də *also* -'bīf-\ *n* : a congenital cleft of the vertebral column with hernial protrusion of the meninges

spina bifida oc·cul·ta \-ə-'kəl-tə\ *n* : a congenital cleft of the spinal column without hernial protrusion of the meninges